

Claim Amendments

1 (original): A method of inducing a mutation in a gene in a eukaryotic cell, wherein the gene is operably linked to a promoter, and wherein the gene is within about two kilobases of the promoter, the method comprising expressing a transgenic activation-induced cytidine deaminase (AID) gene in the cell.

2 (original): The method of claim 1, wherein the gene is also operably linked to an enhancer.

3 (original): The method of claim 2, wherein the enhancer is an immunoglobulin enhancer.

4 (currently amended): The method of ~~any one of claims 1-3~~claim 1, wherein the gene is between 10 bases and 2 kb in the 3' direction from the promoter.

5 (currently amended): The method of ~~any one of claims 1-4~~claim 1, wherein the promoter is an immunoglobulin promoter.

6 (currently amended): The method of ~~any one of claims 1-5~~claim 1, wherein a polyA mRNA of the gene is synthesized in the cell, the polyA mRNA of the gene comprising at least 0.01% of total polyA mRNA in the cell.

7 (original): The method of claim 6, wherein the polyA mRNA of the gene comprises at least 0.1% of total polyA mRNA in the cell.

8 (original): The method of claim 6, wherein the polyA mRNA of the gene comprises at least 0.5% of total polyA mRNA in the cell.

9 (original): The method of claim 6, wherein the polyA mRNA of the gene comprises at least 1% of total polyA mRNA in the cell.

10-12 (canceled)

13 (currently amended): The method of ~~any one of claims 1-12~~claim 1, wherein the AID gene is flanked by a sequence foreign to the cell, wherein the sequence foreign to the cell is at least 200 bp long.

14 (canceled)

15 (original): The method of claim 13, wherein the sequence foreign to the cell is at least 2000 bp long.

16-17 (canceled)

18 (currently amended): The method of ~~any one of claims 1-17~~claim 1, wherein the cell is a yeast cell.

19 (currently amended): The method of ~~any one of claims 1-17~~claim 1, wherein the cell is a vertebrate cell.

20 (original): The method of claim 19, wherein the cell is a mammalian cell.

21 (original): The method of claim 20, wherein the cell is a B-cell.

22 (original): The method of claim 20, wherein the cell is a hybridoma.

23 (currently amended): The method of ~~any one of claims 20-22~~claim 20, wherein the cell is a human cell.

24 (currently amended): The method of ~~any one of claims 1-23~~claim 1, wherein the gene is an antibody gene.

25 (currently amended): The method of ~~any one of claims 1-23~~claim 1, wherein the gene encodes a protein selected from the group consisting of an enzyme, a transcription factor, a cytokine, and a structural protein.

26-33 (canceled)

34 (original): A method of determining the effect of mutations in a gene encoding a protein on the phenotype of the protein in a eukaryotic cell, wherein the gene is operably linked to a promoter, and wherein the gene is within about two kilobases of the promoter, the method comprising

- (a) expressing the protein and a transgenic AID gene in the eukaryotic cell;
- (b) establishing clonal colonies of the cell;
- (c) identifying clonal colonies that produce a gene of the protein that has a mutation;
- (d) determining whether the protein expressed by the mutated gene in any clonal colony identified in step (c) has an altered phenotype; and
- (e) associating the altered phenotype with a particular mutation.

35-57 (canceled)

58 (original): A method of inducing a mutation in an antibody gene in a eukaryotic cell, the method comprising expressing a transgenic AID gene in the cell.

59-96 (canceled)

97 (original): A method of inducing a class switch in an antibody heavy chain gene in a eukaryotic cell, the method comprising expressing a transgenic AID gene in the cell.

98-124 (canceled)

125 (original): A method of altering an affinity or a specificity of a monoclonal antibody to an antigen, or altering a cross-reactivity of the monoclonal antibody to a second antigen, wherein the monoclonal antibody is produced by a eukaryotic cell, and wherein the cell is capable of expressing a transgenic AID gene under inducible control, the method comprising

(a) expressing the AID gene in the eukaryotic cell for a time and under conditions sufficient to induce a mutation in a gene encoding the monoclonal antibody;

(b) suppressing expression of AID gene in the eukaryotic cell;

(c) establishing clonal colonies of the cell; and

(d) determining whether the monoclonal antibody produced by any of the clonal colonies of the cell has altered affinity or specificity to the antigen, or altered cross-reactivity to the second antigen.

126-158 (canceled)

159 (original): A eukaryotic cell comprising a transgenic AID gene, wherein expression of the AID gene is inducible.

160-171 (canceled)

172 (currently amended): The cell of ~~any one of claims 167-169~~claim 159, wherein the cell is a myeloma cell.

173 (currently amended): The cell of ~~any one of claims 167-169~~claim 159, wherein the cell is a hybridoma cell.

174-179 (canceled)

180 (original): A eukaryotic cell expressing an AID gene, wherein the cell is not a B-cell.

181-190 (canceled)

191 (currently amended): The cell of ~~any one of claims 180-190~~claim 180, wherein the cell is a yeast cell.

192 (currently amended): The cell of ~~any one of claims 180-190~~claim 180, wherein the cell is a vertebrate cell.

193 (original): The cell of claim 192, wherein the cell is a mammalian cell.

194 (original): The cell of claim 193, wherein the cell is a human cell.

195-202 (canceled)

203 (original): A myeloma fusion partner expressing an AID gene.

204-212 (canceled)

213 (currently amended): The myeloma fusion partner of ~~any one of claims 203-212~~claim 203, wherein the fusion partner is selected from the group consisting of a Sp2/0-Ag 14, a FOX-NY, a P3X63, NX-1, a P3, a P3X643 Ag8.653, a NS1, and a NSO.

214 (original): A hybridoma expressing an AID gene.

215-261 (canceled)